Remarks

Claims 19-33 and 36-40 are pending in the subject application. By this Amendment, Applicants have canceled claim 39 and amended claim 19. Support for the amendments can be found throughout the subject specification and in the claims as originally filed (see, for example, pages 10-15 and Figures 1-3). Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 19-33, 36-38 and 40 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

At the outset, Applicants respectfully request the courtesy of an interview to discuss this application at the convenience of the Examiner. Applicants also gratefully acknowledge the Examiner's withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Claim 19 is objected to because of informalities. The Examiner indicates the word "either" should not be before "at least one substrate". Applicant gratefully acknowledges the Examiner's careful review of the claims. Applicants have amended claim 19 by deleting the word "either". Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

Claims 19-20, 25-26, 31-33 and 37-38 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Office Action indicates that claim 19 recites "a 'first' minimum medium containing either at least one substrate and a 'second' minimum medium are not supported in the as-filed specification." In addition, the Office Action states that the specification fails to provide an adequate written description of the claim method of testing in parallel the growth capacity of the population of transformed host cells on a first minimum medium containing either at least one substrate {Ai}, as the only source of an element essential to growth and on a second minimum medium containing said product {B} as the only source of an element essential to growth. Applicants respectfully assert that there is adequate written description in the subject specification to convey to the ordinarily skilled artisan that they had possession of the claimed invention.

While the actual terms "first" and/or "second" may not find *ipsis verbis* support in the as-filed specification, Applicants submit that, to fulfill the written description requirement, the disclosure as originally filed does not, however, have to provide a description in the identical words

to support subject matter now claimed. *Cordis Corp. v. Medtronic AVE, Inc.*, 339 F.3d 1352, 1364, 67 USPQ2d 1876, 1885 (Fed. Cir. 2003) ("The disclosure as originally filed does not ... have to provide *in haec verba* support for the claimed subject matter at issue."). For example, pages 12-15 and Figures 2-3 clearly indicate the testing, in parallel, of the ability of the transformed microorganisms to grow on two different minimal medium, one (a first medium) containing at least one substrate (Ai) and another (second) minimal medium containing a product (B). The undersigned would appreciate any suggestion the Examiner may have if this language remains unacceptable upon consideration of this response; however, cancellation of that language should have rendered this issue moot as well. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph, is respectfully requested.

The Office Action also argues that the specification fails to provide adequate written description of the media to be used in the practice of the claimed invention. Specifically, the Office Action states:

> The detail description in the specification, e.g., Example 1 describes species of the media, M9 as applied to a species of substrate/product. The genus claim to a first and second media provides for no definite composition of any media. The claim to a media of undefined composition coupled with any kind of substrate/product covers a limitless number of media apply to any substrate or product. The detail description to a species is inadequate for the genus claim. The law clearly indicates that a patent specification must describe the claimed invention in sufficient detail (not in general terms). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures and formulas to show that the invention is complete.

In this regard, Applicants submit that the as-filed specification clearly complies with the written description requirement. As noted As indicated in *Capon v. Eshhar*, 418 F.3d 1349, 1357, 76 U.S.P.Q.2d 1078, 1084 (Fed. Cir. 2005),

> The "written description" requirement implements the principle that a patent must describe the technology that is sought to be patented; the requirement serves both to satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed. *See Enzo Biochem*, 296 F.3d at 1330 (the written description requirement "is the quid pro quo of the patent system; the public must receive meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time"); *Reiffin v. Microsoft Corp.*, 214 F.3d 1342,

> 1345-46 (Fed. Cir. 2000) (the purpose of the written description requirement "is to ensure that the scope of the right to exclude . . . does not overreach the scope of the inventor's contribution to the field of art as described in the patent specification"); *In re Barker*, 559 F.2d 588, 592 n.4 (C.C.P.A. 1977) (the goal of the written description requirement is "to clearly convey the information that an applicant has invented the subject matter which is claimed"). The written description requirement thus satisfies the policy premises of the law, whereby the inventor's technical/scientific advance is added to the body of knowledge, as consideration for the grant of patent exclusivity.
>
> The descriptive text needed to meet these requirements varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence. The law must be applied to each invention that enters the patent process, for each patented advance is novel in relation to the state of the science. Since the law is applied to each invention in view of the state of relevant knowledge, its application will vary with differences in the state of knowledge in the field and differences in the predictability of the science.

In this case, the definition of minimum medium is known by the skilled person, *i.e.*, a medium containing the minimum nutrients necessary for colony growth. All types of minimum media can be used and the skilled person is able to choose the medium adapted to the cells to be cultured (see, for example, Bergey's Manual of Determinative Bacteriology, a source for such information well-known to those skilled in the art since at least 1957). The only restriction for a medium to be used in the method of claim 19 is that the substrate {Ai} or the product {B} is the only source of an element essential to growth of cells (such as carbon).

Applicants also respectfully note that there is no per se rule that information must be determined afresh when the information is included or known in the prior art and that the Federal Circuit emphasized that a "re-description of what was already known..." has never been required, in contrast to oft-cited cases such as *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997) where the cDNA for human insulin had never been characterized (*Capon v. Eshhar*, 76 U.S.P.Q.2d 1078, 1084-1085 (Fed. Cir. 2005). Accordingly it is respectfully submitted that the as-filed specification complies with the written description requirement with respect to minimum medium that can be used in the practice of the claimed invention and reconsideration and withdrawal of the rejection is respectfully requested.

Claims 19-20, 25-26, 31-33, 37-40 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite. Claim 19, step c), is rejected as being vague and indefinite as to the parallel testing of a

first and second media of the population of transformed host cells containing Ai or B. The Office Action claims that it is unclear as to how the parallel testing of the transformed cells is accomplished both in the two different Ai medium and B medium, especially in the absence of positive support in the original disclosure. Claim 19 is also rejected as being vague and indefinite as to whether growth capacity refers to the amount of transformed host cells being parallel tested in either medium or to the ability of the transformed host cells to grow in two separate medium and as to the differentiating features of the first and second minimum medium or the essential element in Ai or B. The Office Action states that the metes and bounds of each of the media are not clearly set forth in the claim or specification. Applicant respectfully submits that the amendments made to the claims have rendered these issues moot. For example, the issue related to step c has been rendered moot by the cancellation of "first" and "second" in that subsection of the claim.

The issue noted in subsection 2 of the rejection (at page 7), likewise, has been rendered moot by the amendment of the claim to recite that the method tests the ability of said population of transformed host cells to grow on a minimum medium containing at least one substrate {Ai} as the only source of an element essential to growth and testing the ability of said population of transformed host cells to grow on a minimum medium containing a said product {B} as the only source of an element essential to growth. Regarding the issue in point 3, Applicants submit that the claims are not vague and indefinite as the medium contains a substrate or a product of interest (a desired product). Those skilled in the art would have been reasonably apprised as to the meaning of these terms in the context of the as-filed specification; thus, reconsideration and withdrawal of this aspect of the invention is respectfully requested.

Claim 20 is indefinite and inconsistent with claim 20 in the recitation of a "minimum medium". The Office Action notes that claim 19 recites for a first and second minimum media and it is unclear which of the first and second minimum media the broader minimum medium of claim 20 refers to or if this media is different from the first and second media for Ai and B of claim 19. In the context of this rejection, Applicants respectfully submit that one skilled in the art, in view of the teachings of the as-filed specification (see, for example, pages 12-15 and Figures 2 and 3), would have recognized that claim 20 refers to a third medium that contains both Ai and B and that this

medium is separate and distinct from those recited in claim 19. Accordingly, reconsideration and withdrawal of this aspect of the rejection is respectfully requested.

The Office Action indicates that the term "high GC" in claim 39 is a relative term which renders the claim indefinite since it is not defined by the claim and the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear as to the basis by which a library of sequences is considered to be of high GC content one over the other of either the member in a library or the library per se. As indicated above, claim 39 has been canceled thereby making the rejection moot. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested.

Claims 19-20, 25-26, 31-33 and 37-38 are rejected under 35 U.S.C. § 102(b) as anticipated by Hoch *et al.* (U.S. Patent No. 6,368,793). In addition, claims 19-20, 25-26, 31-33 and 37-40 are rejected under 35 USC §102(b) as anticipated by Hoch *et al.* (U.S. Published Application No. 2003/0068807). The Office Action states that the Hoch *et al.* patent discloses a process to identify the metabolic pathway from a source compound (Ai as claimed) to a target compound (B) that involves the creation/identification of an easily genetically-manipulated organism containing an inducible signal, which is activated when a target compound is metabolized. This is followed by the screening of nucleic acid in the organism to identify genes which metabolize the source compound to the target compound. The Office Action indicates that the Hoch *et al.* publication discloses methods of identifying a host cell that encodes a metabolic pathway that converts a precursor molecule into a desired product compound, where steps (a) and (b) are optional, by (a) culturing a population of host cells under conditions that allow expression of the metabolic pathway; (b) assaying the host cells, or extract thereof, for the presence of the desired product compound; and (c) identifying a host cell that contains the desired product compound in the presence, but not in the absence, of the precursor molecule; where an identified host cell from step (c) contains a metabolic pathway that converts the precursor molecule into a desired product compound. A library of expressible nucleic acid molecules is introduced into the population of host cells prior to step (a). The nucleic acid molecules are derived from an environmental source, such as mud, soil. The host cell is a bacterial cell and can be derived from an environmental source. The precursor molecule is e.g., 7-aminocephalosporanic

acid (7-ACA). Hoch *et al.* is also cited as disclosing at *e.g.*, paragraph [0016] that organisms can be identified that contain enzymatic pathways that convert precursor molecules into active compounds. The genes that encode the conversion pathways can be cloned. Alternatively or additionally, methods can be used to isolate and characterize these active compounds from the organism or recombinant organism. The Office Action further notes that Hoch *et al.* disclose at e.g., paragraph [0025] that host cell mean a cell with a metabolic pathway that converts a precursor molecule to a desired product compound. The Office Action concludes that Hoch *et al.* disclose at *e.g.*, paragraph [0039] expression constructs introduced into the appropriate library host organisms. Applicants respectfully assert that the Hoch *et al.* references do not anticipate the claimed invention.

In the present invention, the selection of host cells transformed with a DNA library (in step b) is carried out on a minimum medium comprising a substrate {Ai} as the only source of an essential element and on a minimum medium comprising the product {B} as the only source of an essential element. It is a double selection step that utilizes two separate sets of medium, each of which contains either a substrate {Ai} or a product {B} as the only source of an essential element. In Hoch, the selection of transformed host cells comprising environmental DNA is carried out only on media comprising the source compound (or substrate) S, as illustrated in Fig. 11 or 12. Applicants submit that the Office Action has incorrectly interpreted the meaning of Fig. 11. In that figure, the selection of cells that are capable of metabolizing a target compound "T" (or product) to an essential factor is only used to obtain the tester strain (a strain that has not been transformed with environmental DNA). The tester strain is then transformed with a library of environmental DNA and the screening of these transformed host cells is carried out only on medium comprising the source compound (or substrate) S (2-KLG for the example illustrated on Fig. 12). The aim of this metabolic selection process is to identify the gene of interest that catalyzes the conversion of "S" to "T" in the tester strain (see, for example, the legend of Fig. 11, column 17). Consequently, step c) of claim 19 is not disclosed in this document and claims are, thus, novel over the teachings of the Hoch patent. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. § 102(b) is respectfully requested.

Turning to the rejection as set forth over the Hoch patent application publication, this document relates to a method of identifying a host cell that encodes a metabolic pathway that

converts a precursor molecule (a substrate) into a growth inhibitory compound (the product). This method comprises culturing host cells that have been transformed with a DNA library on a medium containing the precursor and the target cells. Host cells that are capable of inhibiting the growth of the target cells only in presence of the precursor are selected. These selected cells comprise the DNA fragment encoding the metabolic pathway of interest. The screening method disclosed in this document does not comprise any selection step of host cells on a medium into which the inhibitory compound, *i.e.*, product B, as only source of an element essential to growth has been incorporated . Consequently, step c) of claim 19 is not disclosed in this document and the claims are, thus, novel over the teachings of the Hoch patent application publication Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. § 102(b) is respectfully requested.

Claims 19-20, 25-26, 31-33 and 37-38 are rejected under 35 U.S.C. § 103(a) as obvious over Handelsman *et al.* (U.S. Patent No. 7,008,767) in view of Hoch *et al.* (U.S. Patent No. 6,368,793). Applicants respectfully assert that the claimed invention is not obvious over the cited references. The Office Action argues that the claimed invention is obvious over the combined teachings of Handelsman *et al.* and Hoch (U.S. Patent No. 7,008,767). The Office Action states that the comparison of gene products of the transfected host cell to the non-transfected host cell disclosed in Handelsman *et al.* implicitly teach testing transfected host cell by growth on a medium comprising the product. Applicants respectfully disagree with this interpretation of Handelsman *et al.*

Handelsman *et al.* relates to a method for identifying microbial genes involved in biosynthetic pathways. This method comprises transforming host cells with a DNA library and screening said transformed host cells to detect compounds produced by heterologous genes. These heterologous genes can then be identified and cloned. The detection of compounds produced by heterologous genes could involve the comparison of gene products of the transfected host cells to the non-transfected host cells. The assays to detect a new product in a transformed host cells may be carried out using numerous techniques explicitly disclosed in the section VI of this document. Thus, the skilled person who would compare transfected host cells to non-transfected host cells and analyze the compounds produced by these cells as disclosed. The person of ordinary skill in the art, who would like to detect new biosynthetic pathway and thus new compounds encoded by genes from microbial organisms, would not have been motivated to culture transformed cells on a medium

comprising the product of the biosynthetic pathway considering that this method is used for detecting cells that are capable of metabolizing that product as opposed to detecting cells that are capable of producing the product. Thus, Handelsman *et al.* fail to describe or to suggest the screening of transformed host cells on a medium containing the product of the metabolic pathway of interest as the only source of an essential element.

In responding to the arguments presented in the last response, the Office Action argues that Example 1 of Hoch provides teachings demonstrating the obviousness of the claimed invention. In Example 1 of Hoch , a first screening was used to identify strains which could be used to produce a tester strain. This tester strain has to be able to grow on medium containing the product (in the presence of an inducer) and not on medium containing the substrate. A strain that is capable of growing on the product and not on the substrate is then genetically modified in order to make the metabolic pathway allowing the growth on the product inducible. The resulting strain is the tester strain which can be transformed with a DNA library. In Hoch, the screening of transformed host cells is disclosed in Example 3. This screening is carried out in the presence of the substrate and in the presence or the absence of the inducer, but always in the absence of the product. This screening method is detailed in Example 3 and at column 33, lines 5-9 of Hoch: "*This library is then transfected into the tester strain and the resulting pool of transfected cells selected for growth on the source compound (2-KLG in the example)* ***in the absence of the target compound*** *(ascorbate in the example) and the presence of the inducer*" (emphasis added). Thus, Hoch fails to describe or to suggest the screening of host cells transformed with a DNA library on a medium containing the product of the metabolic pathway of interest as the only source of an essential element. Consequently, Hoch cannot remedy the deficiencies of Handelsman *et al.* and the subject-matter of claims would not have been obvious to a person of ordinary skilled in the art. Accordingly, reconsideration and withdrawal of the rejection of record is respectfully requested.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including

any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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